

C2 By "biologically active FREAC3" is meant that the FREAC3 within an individual is sufficient to prevent anterior segment dysgenesis or development/progression of FREAC3-dependent glaucoma in an otherwise-healthy individual. An assessment of the relative FREAC3 biological activity in an individual may be made, e.g., by comparing the FREAC3 sequence in the individual to known wild type and mutant FREAC3 sequences, by measuring the relative amount of FREAC3 binding in a sample to a FREAC3 binding site (e.g., aGTAAA(T/c)AAAcA (SEQ ID NOs: 3 and 4)), or by measuring the relative ability of FREAC3 in a sample to transactivate expression of a FREAC3-dependent gene (e.g., by measuring reporter gene expression from a chimeric gene that contains a FREAC3 binding site in its regulatory region), relative to that of wild-type FREAC3, or by equivalent approaches. Prevention and/or treatment of glaucoma may be effected by increasing the biological activity of a FREAC3 molecule or by increasing the number of FREAC3 molecules in a patient with relatively low FREAC3 biological activity. Preferably, FREAC3 biological activity is at least 25% of that in a normal individual, more preferably, at least 50%, even more preferably, at least 75%, and most preferably, at least 90% of that in a normal individual.

At page 19, lines 3-4:

C3 Fig. 2 is a diagram showing the cDNA and amino acid sequence of FREAC3 (SEQ ID NO: 1).

At page 19, lines 5-6:

C⁴ Fig. 3 is a diagram showing autoradiographs that display the sequences of mutated FREAC3 genes with lanes representing GATC from left to right. The reverse primer sequence is shown in each case for patients (SEQ ID NOs: 8, 10 and 12) and controls (SEQ ID NOs: 7, 9 and 11).

At page 33, line 20, through page 34, line 9:

C⁵ Binding of mutant or wild-type FREAC3 to the FREAC3 *in vitro* binding site sequence (aGTAAA(T/c)AAAc; SEQ ID NOs: 3 and 4) may be used to screen for compounds that modulate FREAC3 biological activity. One method by which to quantitate such changes is by an ELISA-type assay. Samples containing FREAC3 are incubated with test compounds as described above, plus an oligonucleotide encoding a FREAC3 binding site (such as aGTAAA(T/c)AAAc; SEQ ID NOs: 3 and 4) that is affixed to a solid support (e.g., a filter, or a microtiter well). After allowing FREAC3 to interact with its cognate binding sequence and washing away unbound FREAC3, the amount of FREAC3 bound to the immobilized oligonucleotide may be quantitated by subsequent incubation with a labeled antibody. A compound that increases or decreases the amount of mutant FREAC3 bound to the immobilized oligonucleotide indicates a compound that may be useful for the treatment or prevention of glaucoma or anterior segment dysgenesis.